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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/514,070	02/26/2000	Merrill A Biel	22272-14	8621

7590 10/15/2002

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EXAMINER

SHAY, DAVID M

ART UNIT PAPER NUMBER

3739

DATE MAILED: 10/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/514,070

Applicant(s)

Biel

Examiner

d. shay

Group Art Unit

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—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE — 3 — MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on April 26, 2002
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 1-102 is/are pending in the application.
- Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1-102 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

Office Action Summary

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-102 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The originally filed specification is silent regarding "ionophoric properties" and "concentrations having ionophoric properties".

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-102 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims, exactly what is intended to be encompassed by the term "ionophoric properties" is unclear, especially since applicant is identifying these properties with the concentration of the surfactant and with non-ionic surfactants, for the purposes of examination the term will be considered to mean that the surfactant may function to alter a cell membrane to increase permeability thereof, since this is the definition applicant is arguing e.g. in the first paragraph of page 12 of the instant response. Claims 18, 44, and 86 are further indefinite because they merely recite a result which is already supported by substantial materials or acts recited in the independent claims and

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are thus improper under 112, sixth paragraph and not further limiting. In claims 16-18, 23-25, 38-46, 61-65, 73-78, 84 and 85 it is unclear what, further manipulation is intended to be encompassed thereby. In claim 22 it is unclear what further structure is intended to be claimed. Claim 92 is indefinite because it is unclear how the compositions are "adapted to be disposed in proximity to the ... cell site" when there is nothing inherent therein that would prevent such placement thereof also "the pathogen cell site" lacks positive antecedent basis.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1-3, 8 -12, 15, 17, 18, 20, 22, 24, 26-38, 42, 44, 49-53, 60, 61, 65-69, 71, 81-84, 86, 87, 90, 92, 93, 95, 96, and 100 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Lai et al.

See column 6 line 3 to column 19 line 27.

7. Claims 1-3, 6-8, 10-12, 15, 18, 26, 30-32, 37, 39, 44, 45, 48, 49, 51, 52, 80-83, 85-89, 92, 95, 97 and 101 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Nitzan et al.

8. Claims 1, 4, 5, 10, 13, 14, 17, 23, 26-28, 34, 36, 40, 41, 43, 46, 47, 54-57, 59-64, 72-76, 78 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swartz in combination with Nitzan et al and Williams et al. Swartz teaches a method such as claimed except the use of a surfactant. Nitzan et al teach that surfactants, such as PMNP, which is produced from Polymyxin B (see page 10, first column, 3rd paragraph) and thus the product must contain some Polymyxin B, enhance the efficacy

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on gram negative bacteria of photosensitizers which are already highly effective on gram positive bacteria by permeabilizing the membrane of the gram negative bacteria. Williams et al teach the equivalence of methylene blue and hematoporphyrin derivative and the use of surfactants to improve gel properties. It would have been obvious to the artisan of ordinary skill to use the surfactant mixture of Nitzan et al in the method of Swartz, since this would improve gel properties, as taught by Williams et al, and to employ non-ionic and and amphoteric surfactants, since these do not affect the method in a manipulative sense are not critical and provide no unexpected result, thus producing a method and protocol such as claimed.

9. Claims 9, 19-22, 95, 98, and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swartz in combination with Nitzan et al and Williams et al. Swartz teaches employing methylene blue for application to a treatment site. Nitzan et al teach the enhanced effect of photosensitizers used in conjunction with surfactants. Williams et al teach the equivalence of methylene blue and hematoporphyrin derivative and that surfactants improve gel properties. It would have been obvious to the artisan of ordinary skill to include the surfactant mixture of Nitzan et al in the photosensitizer solution of Swartz, since this improves the gel properties, as taught by Williams et al, or alternatively to employ methylene blue as the photosensitizer, since these are equivalents, as taught by Williams et al and to mix the photosensitizer and surfactant, since the surfactant must act on the bacteria prior to the photosensitizer acting thereon, as disclosed by Nitzan et al (see page 89, column 2, first full paragraph); and in either case it would be obvious to use a non-ionic or amphoteric surfactant, since this is not

critical and provides no unexpected result, thus producing a kit or solution such as claimed.

10. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wilk et al in combination with Nitzan et al. Wilk et al teach a method such as claimed except for the combined surfactant and photosensitizing agent. Nitzan et al teach that using a combination of surfactant and photosensitizer can effectively sterilize a variety of harmful bacteria. It would have been obvious to the artisan of ordinary skill to employ a sterilizing solution as taught by Nitzan et al in the method of Wilk et al, since Wilk et al disclose no particular sterilant and the solution of Nitzan et al is highly effective againsts gram positive and gram negative bacteria, thus producing a method such as claimed.

11. Claims 10, 25, 60, 70, 87, and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai et al in combination with Nitzan et al. Lai et al teach a method and treatment protocol such as claimed except for the use of multiple surfactants. Nitzan et al teach a method and treatment protocol as claimed except for the use of multiple photosensitizers. It would have been obvious to the artisan of ordinary skill to employ the hematoporphyrin composition of Lai et al in the method of Nitzan et al since this is very stable formulation, as taught by Lai et al, or alternatively to employ the surfactant of Nitzan et al in the formulation of Lai et al, since this would render the treatment effective against a wide range of bacteria, as taught by Nitzan et al, thus producing a method and treatment protocol such as claimed.

12. Claim 92 and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai et al in combination with Nitzan et al. The teachings of Nitzan et al and Lai et al and the motivations for combination thereof are essentially those already set forth in the rejection of claims 10, 25, 60, 70, 87, and 91 above. Thus it would have been obvious to the artisan of ordinary skill to combine these old and well known teachings to produce a kit such as claimed.

13. Claims 58 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Swartz in combination with Nitzan et al and Williams et al as applied to claims 54 and 72 above, and further in view of Singer et al. Singer et al teach that SDS greatly increase the permeability of cell membranes (see the paragraph spanning pages 113-115). It would have been obvious to the artisan of ordinary skill to employ SDS as the surfactant in the method of Nitzan since this increases the permeability of membranes as taught by Singer et al, which is the function of PMNP in the method of Nitzan et al, thus producing a method such as claimed.

14. Regarding the Nitzan et al reference, applicant argues that "PMNP is not an ionophoric surfactant and this accounts for the limited destruction of gram negative bacteria treated" (emphasis omitted). The examiner respectfully suggests that applicant has misread the Nitzan et al reference. Leaving aside the fact that reference to the ionophoric properties of any surfactant is completely absent both in the instant disclosure and that of the parent, the examiner notes that this term is given its broadest reasonable interpretation consistent with its meaning. Stedman's Medical Dictionary

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defines ionophore as "a compound or substance which forms a complex with an ion and transports it across a membrane" a careful reading of page 90-92 of Nitzan et al (the RESULTS section) clearly states that normally the porphyrin binds only weakly to gram negative cells; that fluorescence analysis of the mixture of PMNP and the porphyrin clearly shows an interaction between the two molecules; and that the two molecules combined drastically increase the amount of porphyrin bound to the cells and the amount of cells killed during PDT. Thus PMNP clearly displays "ionophoric properties" within the broadest reasonable interpretation of the term. There are several other aspects of Nitzan which also bear exploration, however. For example, as can be seen from the third paragraph in column 1 on page 90 of Nitzan et al PMNP is made from Polymyxin B sulfate, thus the compound will inevitably contain some Polymyxin B sulfate and further the PMNP will be Polymyxin B nonapeptide. Thus the Polymyxin B sulfate will act as an ionophoric surfactant and, since applicant is arguing that the Polymyxin B sulfate and Polymyxin B nonapeptide are distinct surfactants, the mixture of Nitzan et al contains a plurality of surfactants. As to the "limited destruction" of the bacteria, while table 1 on page 91 of Nitzan et al does indicate in the neighborhood of one thousand E. coli surviving after 3 hours, an inspection of the adjacent column of this table, which shows the survival fraction clearly demonstrates that well in excess of 99.99% of the bacteria were killed after 3 hours, the examiner respectfully submits that this is a significant portion of the bacteria. It is further noted that the paragraph bridging pages 90 and 91 explicitly states that no viable bacteria were found after 10 hours, this result cannot properly be termed "limited destruction". While applicant asserts that

Nitzan et al teaches away from the concept of using photosensitizers and ionophoric surfactants no teachings of Nitzan et al are proffered to bolster this assertion. Thus, in the face of the clear teachings of Nitzan et al, including but not limited to the explicit discussion of permeabilizing bacteria membranes by PMNP (page 89, column 2, full paragraph) noted by the examiner, applicant's unsupported assertion to the contrary is not convincing.

15. The examiner notes applicant's reference to the terminal disclaimer however there is no such paper currently in the file and until the examiner can evaluate such a submission the double patenting rejection must be maintained and is thus hereby repeated.

16. Applicant's arguments filed April 26, 2002 have been fully considered but they are not persuasive. For the reasons set forth above.

17. Applicant's arguments with respect to claims 1-3, 8-12, 15, 17, 18, 20, 22, 24-38, 42, 44, 49-53, 60, 61, 65-71, 81-84, 86, 87, 90-96, and 100 have been considered but are moot in view of the new ground(s) of rejection.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

.Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Shay whose telephone number is (703) 308-2215. The examiner can normally be reached Tuesday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Linda Dvorak can be reached at (703) 308-0994.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0858.

David Shay:bhw
October 11, 2002

October 10, 2002



DAVID M. SHAY
PRIMARY EXAMINER
GROUP 330